

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: YGUERABIDE et al.
Title: ANALYTE ASSAY USING
PARTICULATE LABELS
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PRELIMINARY AMENDMENT

Commissioner for Patents
Box Patent Application
Washington, D.C. 20231

Sir:

Please amend the application as follows:

In the Specification:

Please amend the specification as follows:

Delete the first paragraph on Page 1, and insert the following paragraph:

This application is a divisional of Yguerabide et al., U.S. Application 08/953,713, filed October 17, 1997, which is a continuation-in-part of Yguerabide et al., U.S. Application 08/844,217, filed April 18, 1997, now U.S. Patent 6,214,560, which claims the benefit of Yguerabide et al., U.S. Provisional Application 60/016,383, filed April 25, 1996, all of which are incorporated herein by reference in their entireties, including drawings.

In the Claims:

Cancel claims 1-48 and insert the following new claims.

1 49. (New) At least one population, each said population comprising a
2 plurality of specifically detectable metal-like light scattering particles,
3 wherein said particles comprise at least one metal-like light scattering
4 material, and
5 wherein said particles have at least one additional material on their surfaces
6 that provides chemical stability and specific binding to an analyte.

7
8 50. (New) The population of claim 49, wherein said material does not
9 significantly interact with light in the visible region of the spectrum.

10
11 51. (New) The population of claim 50, wherein said at least one additional
12 material comprises a protein, nucleic acid or peptide.

13
14 52. (New) The population of claim 50, wherein said at least one additional
15 material comprises a polymer.

16
17 53. (New) The population of claim 50, wherein said at least one additional
18 material is an organic compound or inorganic compound.

19
20 54. (New) The population of claim 50, wherein said at least one additional
21 material comprises a metal.

22
23 55. (New) The population of claim 49, wherein said particles are spherical.

24
25 56. (New) The population of claim 49, wherein said particles are oval or
26 ellipsoidal.

27

28 57. (New) The population of claim 49, wherein said particles are
29 asymmetrical.

30

31 58. (New) The population of claim 49, wherein the coefficient of variation
32 in size of said plurality of particles in a said population is less than 15%.

33

34 59. (New) The population of claim 49, wherein the coefficient of variation
35 in size of said plurality of particles in a said population is less than 10%.

36

37 60. (New) The population of claim 49, wherein the coefficient of variation
38 in size of said plurality of particles in a said population is less than 5%.

39

40 61. (New) The population of claim 49, wherein said particles comprise a
41 surface coat of gold.

42

43 62. (New) The population of claim 49, wherein said particles comprise a
44 surface coat of silver or silver alloy.

45

46 63. (New) The population of claim 49, wherein said particles comprise a
47 metal.

48

49 64. (New) The population of claim 49, wherein said particles comprise gold.

50

51 65. (New) The population of claim 49, wherein said particles comprise a
52 mixed composition of gold and silver.

53

54 66. (New) The population of claim 49, wherein said particles comprise gold
55 and another metal-like material.

56

57 67. (New) The population of claim 49, wherein said particles comprise silver
58 and another metal-like material.

59

60 68. (New) The population of claim 49, wherein said particles comprise gold
61 and a non-metal-like material.

62

63 69. (New) The population of claim 49, wherein said particles comprise silver
64 and a non-metal-like material.

65

66 70. (New) The population of claim 49, wherein said particles comprise silver
67 and a magnetic or ferro electric material.

68

69 71. (New) The population of claim 49, wherein said particles comprise gold
70 and a magnetic or ferro electric material.

71

72 72. (New) The population of claim 49, wherein said particles are composed
73 of a mixture of metal-like materials and a magnetic or ferro electric material.

74

75 73. (New) The population of claim 49, wherein said particles are composed
76 of silver and gold and a magnetic or ferro electric material.

77

78 74. (New) The population of claim 49, wherein said particles have a surface
79 coating.

80

81 75. (New) The population of claim 74, wherein said surface coating is
82 selected from the group consisting of polymer, protein, nucleic acid, and
83 carbohydrate.

84

85 76. (New) The population of claim 49, wherein said particles comprise gold
86 and have an average diameter between 10 and 45 nanometers inclusive.

87

88 77. (New) The population of claim 49, wherein said particles comprise gold
89 and have an average diameter between 50 and 70 nanometers inclusive.

90

91 78. (New) The population of claim 49, wherein said particles comprise gold
92 and have an average diameter between 80 and 120 nanometers inclusive.

93

94 79. (New) The population of claim 49, wherein said particles comprise gold
95 and have an average diameter greater than 120 nanometers and less than one
96 micrometer.

97

98 80. (New) The population of claim 49, wherein said particles comprise silver
99 and have an average diameter between 5 and 50 nanometers.

100

101 81. (New) The population of claim 49, wherein said particles comprise silver
102 and have an average diameter between 20 and 100 nanometers.

103

104 82. (New) The population of claim 49, wherein said particles comprise silver
105 and have an average diameter between 10 and 200 nanometers.

106

107 83. (New) The population of claim 49, wherein said particles comprise silver
108 and have an average diameter of 120 nanometers or less.

109

110 84. (New) The population of claim 49, wherein said particles comprise silver
111 and have a diameter selected from the group consisting of 10, 20, 30, 40, 60, and
112 100 nm.

113

114 85. (New) The at least one population of claim 49, wherein said at least
115 one population is two or more populations, and wherein the particles of each

population are different specifically detectable metal-like light scattering particles that specifically bind to different analytes.

86. (New) The two or more populations of claim 85, wherein said populations have size distributions with coefficients of variation less than 15%.

87. (New) The two or more populations of claim 85, wherein said populations have size distributions with coefficients of variation less than 10%.

88. (New) The two or more populations of claim 85, wherein said populations have size distributions with coefficients of variation less than 5%.

89. (New) A specifically detectable light scattering particle reagent comprising
a population of particles formed from at least one light scattering material selected from the group consisting of a metal, a metal compound, a metal oxide, a semiconductor, and a superconductor,
wherein said particles have an average diameter between 1 and 500 nanometers; and
at least one base molecule bound to the surface of said particle, wherein said base molecule is adapted to bind to a binding agent,
wherein said particle reagent specifically binds to an analyte.

90. (New) The particle reagent of claim 89, wherein said particles further have a stabilizing surface coat.

91. (New) The particle reagent of claim 90, wherein said stabilizing surface coat comprises a polymer.

146 92. (New) The particle reagent of claim 89, wherein said base molecule is
147 bound to said binding agent.

148
149 93. (New) The particle reagent of claim 89, wherein said particles have a
150 plurality of different base molecules bound on the surface of said particles.

151
152 94. (New) The particle reagent of claim 89, wherein said particles comprise
153 a metal.

154
155 95. (New) The particle reagent of claim 89, wherein said particles comprise
156 gold.

157
158 96. (New) The particle reagent of claim 89, wherein said particles comprise
159 silver.

160
161 97. (New) The particle reagent of claim 89, wherein said particles have an
162 additional material on the surface that does not significantly interact with light in the
163 visible region of the spectrum.

164
165 98. (New) The particle reagent of claim 97, wherein said material on the
166 surface is a protein, nucleic acid or peptide.

167
168 99. (New) The particle reagent of claim 97, wherein said material on the
169 surface is a metal.

170
171 100. (New) The particle reagent of claim 89, wherein said particles are
172 spherical.

173
174 101. (New) The particle reagent of claim 89, wherein said particles are oval
175 or ellipsoidal.

176

177 102. (New) The particle reagent of claim 89, wherein said particles are
178 asymmetrical.

179

180 103. (New) The particle reagent of claim 89, wherein said population has a
181 coefficient of variation in size of said particles of less than 15%.

182

183 104. (New) The particle reagent of claim 89, wherein said population has a
184 coefficient of variation in size of said particles of less than 10%.

185

186 105. (New) The particle reagent of claim 89, wherein said population has a
187 coefficient of variation in size of said particles of less than 5%.

188

189 106. (New) The particle reagent of claim 89, wherein said particles
190 comprise a mixed composition of gold and silver.

191

192 107. (New) The particle reagent of claim 89, wherein said particles
193 comprise gold and another metal-like material.

194

195 108. (New) The particle reagent of claim 89, wherein said particles
196 comprise silver and another metal-like material.

197

198 109. (New) The particle reagent of claim 89, wherein said particles
199 comprise gold and a non-metal-like material.

200

201 110. (New) The particle reagent of claim 89, wherein said particles
202 comprise silver and a non-metal-like material.

203

204 111. (New) The particle reagent of claim 89, wherein said particles
205 comprise silver and a magnetic or ferro electric material.

206
207 112. (New) The particle reagent of claim 89, wherein said particles
208 comprise gold and a magnetic or ferro electric material.

209
210 113. (New) The particle reagent of claim 89, wherein said particles
211 comprise a mixture of metal-like materials and a magnetic or ferro electric material.

212
213 114. (New) The particle reagent of claim 89, wherein said particles
214 comprise silver and gold and a magnetic or ferro electric material.

215
216 115. (New) The particle reagent of claim 89, wherein said particles
217 comprise silver and have a diameter selected from the group consisting of 10, 20,
218 40, 60, and 100 nm.

219
220 116. (New) The particle reagent of claim 89, wherein said particles
221 comprise gold and have an average diameter between 10 and 45 nanometers
222 inclusive.

223
224 117. (New) The particle reagent of claim 89, wherein said particles
225 comprise gold and have an average diameter between 50 and 70 nanometers
226 inclusive.

227
228 118. (New) The particle reagent of claim 89, wherein said particles
229 comprise gold and have an average diameter between 80 and 120 nanometers
230 inclusive.

231
232 119. (New) The particle reagent of claim 89, wherein said particles
233 comprise gold and have an average diameter greater than 120 nanometers and less
234 than one micrometer.

236 120. (New) The particle reagent of claim 89, wherein said particles
237 comprise silver and have an average diameter between 5 and 50 nanometers.
238

239 121. (New) The particle reagent of claim 89, wherein said particles
240 comprise silver and have an average diameter between 20 and 100 nanometers.
241

242 122. (New) The particle reagent of claim 89, wherein said particles
243 comprise silver and have an average diameter between 10 and 200 nanometers.
244

245 123. (New) The particle reagent of claim 89, wherein said particles
246 comprise silver and have an average diameter of 120 nanometers or less.
247

248 124. (New) The particle reagent of claim 89, wherein said particles
249 comprise silver and have a diameter selected from the group consisting of 10, 20,
250 30, 40, 60, and 100 nm.
251

252
253 125. (New) A multiparticle optical signal agent comprising
254 at least one particle formed of a magnetic or ferro electrical material,
255 attached to
256 at least one metal-like particle.
257

258 126. (New) The multiparticle optical signal agent of claim 125, wherein at
259 least one said metal-like particle comprises silver or gold.
260
261

262 127. (New) A method for making specifically detectable coated gold
263 particles, comprising:
264 contacting a population of seed particle having a size between about 1 and
265 20 nanometers in diameter with a gold chloride solution and a hydroxylamine

hydrochloride solution under conditions in which the size of the resulting gold particles has a coefficient of variation of less than 10%; and
attaching a specific binding agent or a molecule for binding of a binding agent to said particles.

128. (New) The method of claim 127, wherein the size of said resulting gold particles has a coefficient of variation of less than 5%.

129. (New) The method of claim 127, wherein said resulting gold particles have a diameter of between 10 and 45 nanometers inclusive.

130. (New) The method of claim 127, wherein said resulting gold particles have a diameter of between 50 and 70 nanometers inclusive.

131. (New) The method of claim 127, wherein said resulting gold particles have a diameter of between 80 and 120 nanometers inclusive.

132. (New) The method of claim 127, wherein said resulting gold particles have a diameter of greater than 120 nanometers and less than one micrometer.

133. (New) The method of claim 127, wherein said seed particles are gold.

134. (New) The method of claim 127, wherein said seed particles are silver.

135. (New) A method for making specifically detectable coated silver particles, comprising:

contacting a population of seed particle with a silver salt solution under conditions such that silver is deposited on said seed particles; and

295 attaching a specific binding agent or a molecule for binding of a binding agent
296 to said particles.

297
298 136. (New) The method of claim 135, wherein said seed particles are gold.

299
300 137. (New) The method of claim 135, wherein said seed particles are silver.

301
302 138. (New) The method of claim 135, wherein the resulting particles have
303 an average diameter of 20-100 nm.

304
305 139. (New) The method of claim 135, wherein the resulting particles have
306 an average diameter of 10-200 nm.

307
308 140. (New) The method of claim 135, wherein the size of the resulting
309 particles has a coefficient of variation of less than 15%.

310
311 141. (New) The method of claim 135, wherein the size of the resulting
312 particles has a coefficient of variation of less than 10%.

313
314 142. (New) The method of claim 135, wherein the size of the resulting
315 particles has a coefficient of variation of less than 5%.

316
317
318 143. (New) A test kit, comprising
319 a plurality of at least one type of metal-like light scattering particles,
320 wherein the particles are between 1 and 500 nm in diameter, and wherein different
321 particle types, when present, are adapted to bind to different analytes; and
322 a solid phase array comprising a plurality of binding agents bound at a
323 plurality of spatially addressable spots.
324

325 144. (New) The kit of claim 143, wherein said plurality of binding agents
326 bind to a plurality of different analytes.

328 145. (New) The kit of claim 144, wherein said plurality of binding agents
329 comprises a plurality of nucleic acid molecules.

331 146. (New) The kit of claim 144, wherein said plurality of binding agents
332 comprises a plurality of antibodies.

334 147. (New) The kit of claim 144, wherein said plurality of binding agents
335 comprises a plurality of receptors.

337 148. (New) The kit of claim 144, wherein said plurality of binding agents
338 comprises a plurality of proteins.

340 149. (New) The kit of claim 144, wherein said plurality of binding agents
341 comprises a plurality of peptides.

343 150. (New) The kit of claim 144, wherein said plurality of binding agents
344 comprises a plurality of pharmaceutical agents.

346 151. (New) The test kit of claim 143, wherein said at least one metal-like
347 light scattering particle type comprises a plurality of distinguishable particle types.

349 152. (New) The test kit of claim 143, wherein said at least one metal-like
350 light scattering particle type comprises a plurality of distinguishable metal light
351 scattering particle types.

353 153. (New) The test kit of claim 152, wherein each of said plurality of
354 different particle types provides a different color of scattered light on illumination
355 with white light.
356

357 154. (New) The test kit of claim 143, wherein the particles of a particle
358 type have on their surfaces a binding agent that binds to an analyte.
359

360 155. (New) The test kit of claim 143, wherein the particles of a particle
361 type are adapted to indirectly bind to an analyte.
362

363 156. (New) The test kit of claim 143, wherein the particles of a particle
364 type comprise gold.
365

366 157. (New) The test kit of claim 143, wherein the particles of a particle
367 type comprise silver.
368

369 158. (New) The test kit of claim 143, wherein the particles of a particle
370 type comprise gold and silver.
371

372
373 159. (New) A test kit, comprising
374 a plurality of populations of different distinguishable metal-like light scattering
375 particle types, wherein the particles are between 1 and 500 nm and different
376 particle types are adapted to bind to different analytes.
377

378 160. (New) The test kit of claim 159, wherein the particles of a particle
379 type comprise a binding agent that binds to an analyte.
380

381 161. (New) The test kit of claim 159, wherein the particles of a particle
382 type are adapted to indirectly bind to an analyte.

383

384 162. (New) The test kit of claim 159, wherein the particles of a particle
385 type comprise gold.

386

387 163. (New) The test kit of claim 159, wherein the particles of a particle
388 type comprise silver.

389

390 164. (New) The test kit of claim 159, wherein the particles of a particle
391 type comprise gold and silver.

392

393 165. (New) The test kit of claim 159, wherein each of said plurality of
394 populations of different particle types provides a different color of scattered light on
395 illumination with white light.

396

REMARKS

Support for the preceding new claims is provided in the original claims, in the claims of the related provisional application, and in the specification. Thus, no new matter is presented.

Applicant believes that the present application is now in condition for allowance. Favorable consideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Respectfully submitted,

Date

16 August 2001

By

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